

## REMARKS

Claims 29–34 and 36–42 are pending.

### Amendment to the Drawings

Please replace Figure 5 with the attached figure. Figure 5 is amended to correct a typographical error. In the original figure, the nucleic acid and protein sequences were truncated at amino acid 194. The replacement figure includes amino acids 195–198 and the “stop” codon “TAA”. This amendment is made to align Figure 5 with the sequence listing.

Applicants submit that the above amendment does not represent new matter as it merely corrects an obvious typographical error. The sequence of p27 was well known to skilled artisans at the time of filing of the priority application to which the present application claims priority.

In support of this position, applicants submit the relevant pages of PCT publication WO 9602140A1, which is cited on page 7 at line 23 as describing cDNA encoding p27. This application has a publication date of February 1, 1996, which is before the priority date of the present application. Page 17 of the WO 9602140A1 publication states that Figures 15A and 15B list the cDNA sequence and encoded sequence of human kip1 (p27). Figure 15B shows the encoded sequence as consisting of 198 amino acids. Amended Figure 5 correctly shows the previously known sequences for the cDNA and encoded sequences of p27.

### **Sequence Listing**

In response to the request for a paper and computer readable form sequence listing, applicants include a statement that the computer readable form in this application is identical with that filed in application number 08/897,333, filed June 1, 2000. Applicants request that the computer readable form filed in that application be used as the computer readable form for the instant application.

Applicants also include a paper copy of the Sequence Listing filed in application number 08/897,333. The content of this paper copy and the computer readable form are the same and contain no new matter. Applicants request that the Sequence Listing be entered into the specification.

### **Rejection Under 35 U.S.C. §112, second paragraph**

Claims 29-34 and 36-42 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Claim 1 is considered unclear as to whether the nucleic acid is administered with the balloon catheter.

The applicants respectfully traverse this rejection. However, to speed up prosecution and without prejudice or disclaimer of the subject matter claimed therein, the applicants amend claim 29 to recite that the balloon catheter is for administration of the nucleic acid. This amendment contains no

new matter and is supported, *inter alia*, by the specification at page 12, lines 16-17. Applicants submit that this amendment overcomes the 35 U.S.C. §112, second paragraph, rejection and respectfully request that the withdrawal of this rejection.

### Conclusions

Applicants have overcome each of the Examiner's rejections. The application is therefore in condition for allowance and early notice to this effect is earnestly solicited. If, for any reason, the Examiner is unable to allow the application and feels that an interview would be helpful to resolve any remaining issues, he is respectfully requested to contact the undersigned attorney at (312) 321-4229.

Respectfully submitted,

Dated: OCTOBER 12, 2004

John Murray

John Murray, Ph.D.  
Registration No. 44,251  
Attorney for Applicants

BRINKS HOFER GILSON & LIONE  
P.O. BOX 10395  
CHICAGO, ILLINOIS 60610  
Telephone: (312) 321-4200

**Amendments to the Drawings:**

The attached sheet of drawings includes the amendments to Figure 5 and replaces the original sheet including Figure 5.

Attachment: Replacement Sheet

PCT

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INTERNATIONAL APPLICATION PUBLISHED U

(51) International Patent Classification 6 :		A1	WO 9602140A1
A01N 61/00, 63/00, A61K 31/00, 48/00, C07H 21/04, C07K 1/00, C12N 1/00, 5/00, 15/00, C12P 21/06, C12Q 1/00			(43) International Publication Date: 1 February 1996 (01.02.96)
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(22) International Filing Date: 7 June 1995 (07.06.95)			(74) Agent: WHITE, John, P.; Cooper & Dunham LLP, 1185 Avenue of the Americas, New York, NY 10036 (US).
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(71) Applicants (for all designated States except US): SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH [US/US]; 1275 York Avenue, New York, NY 10021 (US). FRED HUTCHINSON CANCER RESEARCH CENTER [US/US]; 1124 Columbia Street, Seattle, WA 98104 (US).			
(72) Inventors; and (75) Inventors/Applicants (for US only): MASSAGUE, Joan [US/US]; Apartment 23A, 1235 York Avenue, New York, NY 10021 (US). ROBERTS, James, M. [US/US]; 2540 Shoreland Drive South, Seattle, WA 98144 (US). KOFF, Andrew [US/US]; Apartment 13R, 504 East 63rd Street,			

(54) Title: ISOLATED p27 PROTEIN AND METHODS FOR ITS PRODUCTION AND USE

(57) Abstract

An isolated protein designated p27 is disclosed. The p27 protein has an apparent molecular weight of about 27 kD, and is capable of binding to and inhibiting the activation of a cyclin E - Cdk2 complex. A nucleic acid sequence encoding p27 protein is disclosed, as well as a method for producing p27 in cultured cells. *in vitro* assays for discovering agents which effect the activity of p27 are also provided. Methods of diagnosing and treating hypoproliferative and hyperproliferative disorders are provided.

Kip1.

Figures 11A and 11B

Kip1 inhibits activation of Cdk2 in vitro. Extracts from 5 exponentially growing A549 cells where incubated with baculovirally expressed histidine-tagged cyclin E alone or together with Kip1. Cyclin E complexes were then retrieved with Ni<sup>++</sup>-NTA-agarose, and assayed for histone H1 kinase activity (A), and by western immunoblotting 10 using anti-Cdk2 antibody (B). Kinase activity was quantitated by Phosphorimager and expressed as arbitrary units. In B, Cdk2\* indicates the faster migrating form of Cdk2 that corresponds to Cdk2 phosphorylated at Thr<sup>160</sup> (Gu et al., 1992).

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Figures 12A and 12B

Expression pattern of Kip1 in various tissues and cell proliferation states. Kip1 Northern blots using equal amounts of poly(A)<sup>+</sup> RNA from the indicated human tissues 20 (A) or from Mv1Lu cells in different proliferation states (B). The latter blot was rehybridized with a glyceraldehyde-phosphate dehydrogenase probe.

Figures 13A and 13B

25 Mink Kip1 cDNA and the encoded mink kip1

Figures 14A and 14B

Mouse Kip1 cDNA and the encoded mouse kip1

30 Figures 15A and 15B

Human Kip1 cDNA and the encoded human kip1

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FIGURE 15A

ATG	TCA	AAC	GTC	CGA	GTC	TCT	AAC	GGG	AGC	CCT	AGC	CTG	GAG	CGG	ATG	48
Met	Ser	Asn	Val	Arg	Val	Ser	Asn	Gly	Ser	Pro	Ser	Leu	Glu	Arg	Met	15
1																
GAC	GCC	AGG	CAG	GCG	GAG	CAC	CCC	AAG	CCC	TGG	GCC	TGC	AGG	AGC	CTC	96
Asp	Ala	Arg	Gln	Ala	Glu	His		Pro	Lys	Pro	Ser	Ala	Cys	Arg	Asn	Leu
																30
TTC	GGC	CCG	GTC	GAC	CAC	GAA	GAG	TAA	ACC	CGG	GAC	TTC	GAG	AGC	CAC	144
Phe	Gly	Pro	Pro	Val	Asp	His	Glu	Glu	Leu	Thr	Arg	Asp	Leu	Glu	Lys	His
																35
TGC	AGA	GAC	ATG	GAA	GAG	GCG	AGC	CAG	CGG	AGC	TGG	AAT	TTC	GAT	TTT	192
Cys	Arg	Asp	Met	Glu	Glu	Ala	Ser	Gln	Arg	Lys	TTP	Asn	Phe	Asp	Pho	
																50
CAG	AAT	CAC	AAA	CCC	CTA	GAG	GGC	ANG	TAC	GAC	TGG	CAA	GAG	GTG	GAG	240
Gln	Asn	His	Lys	Pro	Leu	Glu	Gly	Lys	Tyr	Glu	TTP	Gln	Glu	Val	Glu	
																65
AAG	GGC	AGC	TTC	CCC	GAG	TTC	TAC	TAC	AGA	CCC	CCG	CCC	CCC	AAA	288	
Lys	Gly	Ser	Leu	Pro	Glu	Phe	Tyr	Tyr	Arg	Pro	Pro	Arg	Pro	Pro	Lys	
																95
GGT	GCC	TGC	AAG	GTG	CCG	GCG	CAG	GAG	AGC	CAG	GAT	GTC	AGC	GGG	AGC	336
Gly	Ala	Cys	Lys	Val	Pro	Ala	Gln	Glu	Ser	Gln	Asp	Val	Ser	Gly	Ser	
																100
																110

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## FIGURE 15B

CGC CCG GCG GCG CCT TTA ATT GGG GCT CCC GCT AAC TCT GAG GAC ACC	384
Arg Pro Ala Ala Pro Leu Ile Gly Ala Pro Ala Asn Ser Glu Asp Thr	
115 120 125	
CGT TTG GTC GAC CCA MAG ACT GAT CCT CCG TCG GAC AGC CAG ACG GGG TTA	432
His Leu Val Asp Pro Lys Thr Asp Pro Ser Asp Ser Gln Thr Gly Leu	
130 135 140	
GGG GAG CAA TGC GCA GGA ATA AGG MAG CGA CCT GCA ACC GAC GAT TCT	480
Ala Glu Gln Cys Ala Gly Ile Arg Lys Arg Pro Ala Thr Asp Asp Ser	
145 150 155 160	
TCT ACT CAA AAC AAA AGA GCC AAC AGA ACA GAA GAA AAT GTF TCA GAC	528
Ser Thr Gln Asn Lys Arg Ala Asn Arg Thr Glu Asn Val Ser Asp	
165 170 175	
SGT TCC CCA AAT GCC GGT TCT GTC GAG CAG CCC AAG AAC CCT GGC	576
Gly Ser Pro Asn Ala Gly Ser Val Glu Gln Thr Pro Lys Lys Pro Gly	
180 185 190 195	
CTC AGA AGA CGT CAA ACC TA	597
Leu Arg Arg Arg Gln Thr	
195	

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